Rheumatoid Arthritis is Associated with Higher Prevalence of Thyroid Abnormalities- A Cross-Sectional Study

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ABSTRACT

Background: The relationship between thyroid abnormalities and rheumatoid arthritis is a debatable subject. Studies show a higher prevalence of thyroid abnormalities in patients with RA. It is widely observed that disorders with an autoimmune pathogenesis occur with increased frequency in patients with a history of another disease. RA is a systemic disorder that can affect any organ in the body, it could be speculated that abnormal thyroid functions are due to thyroid activity of the autoantibodies produced in this disease. Objectives:-Present study was doneto study the prevalence and correlation between Rheumatoid Arthritis and thyroid dysfunction; hypo as well as hyperthyroidism and to find whether thyroid disorders are found with increased frequency in Rheumatoid Arthritis patients as compared to general population. Methods: A cross sectional observational study was conducted on 50 patients of RA (diagnosed according to 2010 ACR/EULAR criteria) attending outdoor or admitted in wards at Rajindra hospital Patiala. Age and sex matched 50 persons from general population were taken as control group. These patients were evaluated for thyroid abnormalities using thyroid function test T3, T4, TSH. Results: Thyroid abnormalities were found among 28% cases of RA as compared to 8% among controls. Percentage of clinical hypothyroidism, subclinical hypothyroidism, and clinical hyperthyroidism in cases was 10%, 16%, 2% respectively. In controls percentage of clinical and subclinical hypothyroidism observed was 2% and 6% respectively. Females with RA had two fold enhances prevalence of thyroid abnormalities as compared to males with RA (31.6% females and 16.7% males with RA had thyroid abnormalities). Conclusion: The asymptomatic or mildly symptomatic clinical course of thyroid diseases in RA patients may be masked by underlying disease, posing hazards of late diagnosis and treatment. So higher prevalence of thyroid abnormalities in RA patients in comparison to controls indicate the need for screening by thyroid function tests.

Keywords: Rheumatoid arthritis, Thyroid abnormalities.

INTRODUCTION

For several decades an increased occurrence of thyroid disorders in patients suffering from RA has been documented—both autoimmune and non-autoimmune in nature. In addition, rheumatologic and non-rheumatologic manifestations of AITD have also been studied. It has been widely observed that disorders with an autoimmune pathogenesis occur with increased frequency in patients with a history of another autoimmune disease called (AD) known as polyautoimmunity. Autoimmune disorders share similar mechanisms. Genetic background is, therefore, an important aspect in autoimmunity. [1-14] In AITD, numerous genes have been found to confer risk for the disease including HLA gene complex, CD40, CTLA4, PTPN22, TSH receptor gene, and

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Dr Vijay Kumar, Associate Professor, Department of General Medicine, #5576, Sec-38 Chandigarh. thyroglobulin gene. [6,8-10] CD40, CTLA4, and PTPN22 genes as well as the HLA gene complex have also been implicated in the pathogenesis of RA.[8-10] In addition, shared environmental factors such as smokinghave been implicated in numerous studies as risk factors for AITD and for RA.[15] Several studies have consistently mentioned association and clustering between autoimmune disorders. Α hormonal dysfunction autoimmune thyroid disease (ATD) are present in 6% to 33.8% patients with rheumatoid arthritis (RA).[16] The prevalence of AITD in the general population varies between countries. Prevalence has been described of 5 to 15% in women to 1-5% in men.[17] The concomitant presence of these diseases is more frequent in women than men.

Objectives

Present study was done to study the prevalence and correlation between Rheumatoid Arthritis and thyroid dysfunction; hypo as well as hyperthyroidism and to find whether thyroid

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disorders are found with increased frequency in Rheumatoid Arthritis patients as compared to general population.

MATERIALS AND METHODS

A cross sectional study comparing the prevalence of thyroid dysfunction in RA patients and age and sex matched general population was conducted in patients attending medicine OPD and admitted in medicine wards at Rajindra hospital Patiala.

Inclusion Criteria

GROUP A:- 50 patients between 20-55 years of age who are already diagnosed cases of RA and on treatment for the same and New cases that satisfy 2010 ACR/EULAR criteria for RA.

Group B:- Control Group of 50 age and sex matched patients without RA presenting with unrelated minor ailments.

Exclusion Criteria

- 1) Below 20 years of age
- 2) Above 55 years of age
- 3) Patients having type 2 Diabetes Mellitus
- 4) Other autoimmune diseases as SLE, Addison's disease, systemic sclerosis, scleroderma, allergies.
- 5) Patients with immune-compromised states as AIDS, on chemotherapy.
- 6) Patients with known thyroid disease, under thyroid hormone treatment, any disease known to affect thyroid function i.e. pituitary adenoma and pregnant women.

Patients fulfilling the inclusion criteria were involved in the study. Purpose of study was explained and informed consent was taken from patients and family in their vernacular language. A detailed history, clinical examination and laboratory workup was done.

1) Clinical examination: Medical history taking (including history regarding RA, thyroid diseases and its familial occurrence), physical examination and musculoskeletal system assessment

2) Laboratory tests:-

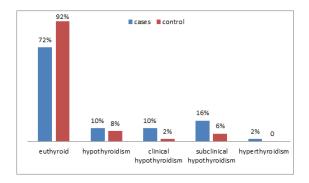
- To evaluate RA activity: erythrocyte sedimentation rate (ESR), Creative protein (CRP)
- Tests for thyroid function: Thyroid stimulating hormone (TSH), serum tri-iodothyronine (T3), serum thyroxine (T4)

RESULTS

 Maximum number of cases was present in age group of 51-55 years and maximum number of controls were in age group of 46-55 years. In our study mean age of presentation was found to be 46.94±8.13 years in RA group and 44.3±9 years in control group. In RA group 24% were males and 76% were

- females. In control group 20% were males and 80% were females
- Mean hemoglobin in cases (RA) was 10.25±1.6 g/dl and in control group was 11.36±1.41 g/dl. The difference among two groups is statistically significant (p<0.001). Low hemoglobin values were observed among RA patients as compared to general population.
- ESR was raised in 90% cases and normal in 10% in RA patients. In control group ESR was raised only in 4% individuals. CRP was positive among 92% RA patients while 8% were negative for CRP. None of the persons from control group had positive CRP.
- Out of 50 patients with RA 88% were positive for Rheumatoid Factor (RA Factor).6 cases of RA negative for RA factor were positive for anti- CCP.
- Among 50 patients of RA thyroid abnormalities were seen in 28% cases while 72% were euthyroid. Hypothyroidism was seen in 26% cases out of which 10% had clinical and 16% had subclinical hypothyroidism. Hyperthyroidism was seen in 2% cases of RA.
- In control population 92% were euthyroid. Clinical hypothyroidism was seen in 2% and subclinical hypothyroidism was seen in 6% of control population. No case of hyperthyroidism was observed in control group.
- 16.67% of male patients with RA had hypothyroidism. 28.95% of all the female patients with RA were hypothyroid while 2.63% of the female patients were hyperthyroid. Thyroid abnormalities were seen more in female patients as compared to male patients with RA.

Thyroid status	Cases (RA)		Control	
	Number	%	Number	% age
		age		
Euthyroid	36	72%	46	92%
Hypothyroid	13	26%	4	8%
a) Clinical	5	10%	1	2%
b) Subclinical	8	16%	3	6%
Hyperthyroid	1	2%	0	0
Clinical	1	2%	0	0
Subclinical	0	0	0	0
Total	50	100%	50	100%



DISCUSSION

RA is a systemic disorder that can affect any organ in the body, it could be speculated that abnormal

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thyroid functions are due to thyroid activity of the autoantibodies produced in these diseases. Various studies conducted worldwide show prevalence of thyroid abnormalities in RA ranging from 0.5% in Morocco to 27% in Slovakia. [18,19]

The present study is conducted with an aim to know whether thyroid dysfunctions are more prevalent in patients with RA or not. Possible explanation of higher prevalence of autoimmune disorders in women is given by sex hormone difference. Estrogen, progesterone and testosterone mediate most of the sex biased differences in immune response. [20] Mean haemoglobin values observed among cases was 10.25±1.6 g/dl and in control group was 11.36±1.41 g/dl. Low haemoglobin values in RA patients were seen in many studies as Smyrnova et al (2014),[21] and Eshnurzaeva et al (2015).[22] Low haemoglobin is explainable because of anaemia of chronic disease and use of DMARDS by RA patients being studied. Most common thyroid abnormality found in this study was subclinical hypothyroidism that was found in 16% RA patients followed by clinical hypothyroidism seen in 10% cases and hyperthyroidism in 2% cases. Similar results were seen in studies conducted by Haghighi et al (2009),^[23] Mir Nadeem et al (2017).^[24] Studies conducted by by Raterman et al (2008),[26] J D Phulkan et al (2016),^[25] Kiran Tandia et al (2016),^[27] show higher prevalence of clinical hypothyroidism over subclinical hypothyroidism.

The most common thyroid dysfunction in present study was subclinical hypothyroidism seen in 16% cases, which according to the literature is present in 9.4% - 21% of patients with RA. In our study thyroid abnormalities were found among 28% cases of RA and 8 % control population. Results of this study are similar to study conducted by Shiroki et al (1993), [28] in which prevalence of thyroid abnormalities among RA patients and controls was 30%, 11% respectively. A similar study by Hala H. Mosli et al (2014), [29] show prevalence of 26.3% in RA and 11% in control group.

There is almost threefold enhanced prevalence of thyroid abnormalities in RA patients in comparison the general population. Subclinical with and hypothyroidism was twofold clinical hypothyroidism was five times more prevalent in RA when compared with general population. The asymptomatic or mildly symptomatic clinical course of thyroid diseases in RA patients may be masked by underlying disease, posing hazards of late diagnosis and treatment, which has also been noticed previously.

CONCLUSION

The asymptomatic or mildly symptomatic clinical course of thyroid diseases in RA patients may be masked by underlying disease, posing hazards of late diagnosis and treatment. Higher prevalence of

thyroid abnormalities in RA patients in comparison to controls indicates the need for screening by thyroid function tests. Keeping in view of the importance of thyroid abnormalities in patients with RA, thyroid examination and thyroid function tests should be done in all RA patients.

REFERENCES

- J. M. Anaya, A. Rojas-Villarraga, and M. Garc´ıa-Carrasco, "The autoimmune tautology: from polyautoimmunity and familial autoimmunity to the autoimmune genes," Autoimmune Diseases, vol. 2012, Article ID 297193, 2 pages, 2012
- M. FallenaZonana, E. Reyes, and A. K. Weisman, "Coexistence of four autoimmune diseases in one patient: the kaleidoscope of autoimmunity," Journal of Clinical Rheumatology, vol. 8, no. 6, pp. 322–325, 2002.
- A. Rojas Villarraga, J. Amaya Amaya, A. Rodriguez Rodriguez, R. D. Mantilla, and J. M. Anaya, "Introducing poly autoimmunity: secondary autoimmune diseases no longer exist," Autoimmune Diseases, vol. 2012, Article ID 254319, 9 pages, 2012.
- J. M. Anaya, J. Castiblanco, A. Rojas-Villarraga, R. PinedaTamayo, R. A. Levy, J. G´omez-Puerta et al., "The multiple autoimmune syndromes. A clue for the autoimmune tautology," Clinical Reviews in Allergy and Immunology. In press.
- L. Punzi and C. Betterle, "Chronic autoimmune thyroiditis and rheumatic manifestations," Joint Bone Spine, vol. 71, no. 4, pp. 275–283, 2004.
- D. A. Chistiakov and R. I. Turakulov, "CTLA-4 and its role in autoimmune thyroid disease," Journal of Molecular Endocrinology, vol. 31, no. 1, pp. 21–36, 2003.
- L. H. Duntas, "Environmental factors and thyroid autoimmunity," Annalesd'Endocrinologie, vol. 72, no. 2, pp. 108–113, 2011.
- 8. Y. Tomer, "Genetic susceptibility to autoimmune thyroid disease: past, present, and future," Thyroid, vol. 20, no. 7, pp. 715–725, 2010.
- Y. Tomer and T. F. Davies, "Searching for the autoimmune thyroid disease susceptibility genes: from gene mapping to gene function," Endocrine Reviews, vol. 24, no. 5, pp. 694– 717, 2003.
- Y. Tomer and A. Huber, "The etiology of autoimmune thyroid disease: a story of genes and environment," Journal of Autoimmunity, vol. 32, no. 3-4, pp.2009; 231–239.
- Becker KL, Ferguson RH, McConahey W.M. The connectivetissue diseases and symptoms associated with Hashimoto's thyroiditis. N Engl J Med 1963; 268:277-80.
- 12. Lazurova I, Benhatchi K, Rovensky J, Kozakova D, Wagnerova H, Tajtakova M et al. Autoimmune thyroid disease and autoimmune rheumatic disorders: a two-sided analysis. Ann N Y AcadSci 2009; 1173:211-6.
- Somers EC, Thomas SL, Smeeth L, Hall AJ. Are individuals with an autoimmune disease at higher risk of a second autoimmune disorder? Am J Epidemiol 2009; 169(6):749-55.
- J. M. Anaya, J. Castiblanco, G. J. Tob'on et al., "Familial clustering of autoimmune diseases in patients with type 1 diabetes mellitus," Journal of Autoimmunity, vol. 26, no. 3, pp. 208–214, 2006.
- 15. Symmons DP, Bankhead CR, Harrison BJ, Brennan P, Barrett EM, Scott DG et al. Blood transfusion, smoking, and obesity as risk factors for the development of rheumatoid arthritis: results from a primary care-based incident case-control study in Norfolk, England. Arthritis Rheum 1997; 40(11):1955-61.
- 16. Silman AJ, Ollier WER, Bubel MA. Autoimmune thyroid disease and thyroid autoantibodies in

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- rheumatoid arthritis patients and their families. Br J Rheum. 1989; 28: 18-21.
- Caron P, Lassoued S, Dromer C, Prevalence of thyroid abnormali ties in patients with rheumatoid arthritis. Thyroidology. 1992; 4: 99-102.
- MałgorzataPrzygodzka, Anna FilipowiczSosnowska. Prevalence of thyroid diseases and antithyroid antibodies in women with rheumatoid arthritis Pol Arch Med Wewn. 2009; 119 (1-2): 39-44.
- S. Benamour, B. Zeroual, L. Fares, H. El Kabli, and S. Bettal, "Rheumatoid arthritis in morocco," Revu du Rhumatisme et des maladies osteo-Articulaires, vol. 59, no. 12, pp. 801-807, 1992.
- Esdaile JM. Exogenous female hormones and rheumatoid arthritis: a methodological view of the contradictions in the literature. British journal of rheumatology. 1989;28Suppl 1:4-10; discussion 8-23.
- 21. Ganna, Smyrnova. The prevalence of anemia in rheumatoid arthritis. Revistabrasileria de rheumatologia, 54(4),257-259.
- Aida Eshmurzaeva, MarifKarimov, IskanderMavlyanov, Marina Sibirkina, NigoraTukhtaeva, BekhzodAbdullaev. The incidence of anemia in patients with rheumatoid arthritis. British Journal of Medicine and Medical Research, ISSN; 2231-0614, vol 13, issue:11
- Haghighi A, Prevalence of thyroid disorders in Systemic Lupus Erythematosus and Rheumatoid Arthritis. Iranian J endocrinology & Metabolism 2009; 11 (1); 49-55.
- 24. Dr Mir Nadeem, Prof AbKhaliq, DrMohd Hayat Bhat, DrFarhat Mustafa, DrMuzaffarMushtaq, Dr Mir Waseem. Thyroid Dysfunction in Rheumatoid Arthritis. Journal of medical science and clinical research JMSCR:November 2016; vol 05: issue 11; page 31028-31036
- 25. J D Phukan, S K Baruah, B K Choudhury, K S Saudaga. Thyroid Dysfunction in Rheumatoid Arthritis. Assam Journal of Internal Medicine; jan, 2008; VOI. 8 Issue 1; P 17-19.
- H. G. Raterman, V. P van Halm, A.E. Voskuyl, S. Simsek, B.A.C Dijkmans, M.T. Nurmohamed. Rheumatoid arthritis is associated with a high prevalence of hypothyroidism which amplifies its cardiovascular risk. Annals of the Rheumatic diseases. 2008;67(2):229-32.
- KiranTandia ,ShikhaAgrawal. Study of Thyroid Dysfunction in Patients with Rheumatoid Arthritis IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN;Feb. 2016:2279-0861.Volume 15, Issue 2 Ver. X, PP 81-84.
- Jeffrey B Shiroky, Martin Cohen, Marie-Louise Ballachey, Carolyn Neville; Thyroid dysfunction in rheumatoid arthritis: a controlled prospective survey. Annals of the Rheumatic Diseases 1993; 52: 454-456.
- Hala H. Mosli and Suzan M. Attar. Prevalence and Patterns of Thyroid Dysfunction in Patients with Rheumatoid Arthritis. The Open Endocrinology Journal, 2014, 7, 1-5.

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